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THE INTERACTIONS IN SURFACTANT SOLUTIONS
BY NMR METHODS

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Avhandling för teknisk doktorsexamen

Avhandlingen kommer att försvaras vid en offentlig
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Gunnilla Clifberg-Larsson
Techn. Lic., MSc

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Gunilla Gillberg - La Force

The Swedish Institute for Surface Chemistry, Stockholm

Div. Phys. Chem. 2, The Lund Institute of Technology, Lund

In this article some results of applying NMR techniques to solutions containing surface active agents will be presented. The following papers will be discussed and they will be referred to with Roman numerals.

- I Eriksson, J. C., and Gillberg, G.,
NMR - Studies of the Solubilization of Aromatic Compounds in Cetyltrimethylammonium Bromide Solution II,
Acta Chem. Scand. 20, 2019 (1966).
- II Gillberg, G., and Ekwall, P.,
Properties and Structure of the Decanolic Solutions in the Sodium Caprylate - Decanol - Water System III.
An NMR Investigation of the Solutions.
Acta Chem. Scand. 21, 1630 (1967).
- III Gillberg, G., Lehtinen, H., and Friberg, S.,
NMR and IR Investigation of the Conditions Determining the Stability of Microemulsions.
J. Colloid Interface Sci. 33, 40 (1970).
- IV La Force, G., and Sarthz, B.,
A Study of the Isotropic Phase in the Ternary System n-Octylamine - p-Xylene - Water Using NMR and Light Scattering
J. Colloid Interface Sci. 37, 254 (1971).
- V Gillberg-La Force, G., and Forsén, S.,
The Binding of Anionic Surfactants to Human Serum Albumin Studied by Means of ^{81}Br Nuclear Magnetic Resonance.
Biochem. Biophys. Res. Commun. 38, 137 (1970).

1. Introduction

The first NMR experiment in surface and colloid chemistry was reported in 1959 by Mc Donald (1), who studied the high resolution proton magnetic resonance spectra of two and three component systems of amphiphilic molecules and water. Since then chemical shifts measurements in proton (I-IV, 1-10), fluorine-19 (11-15) and carbon-13 magnetic resonance (16, 17) and different types of nuclear magnetic relaxation studies (II, V, 17-25) have been used for elucidating interactions between and mobility of the molecules in various isotropic and mesomorphic phases formed in systems containing surface active agents.

2. Some properties of Surfactant Solutions

A surface active molecule consists of one hydrophobic and one hydrophilic region. The hydrophobic or lipophilic part is in general an alkyl or alkylaryl chain, the hydrophilic part one or several polar groups (ionic or nonionic). It is this dual (amphiphilic) nature of the surface active molecules which is responsible for their absorption at water-air and water-oil interfaces and their formation of associated structures such as micelles and various mesomorphic phases (26). In this article mesomorphic phases will not be treated.

When a surfactant is added to water very sharp changes in different physical chemical properties such as the osmotic pressure, the turbidity, the conductivity and the surface properties are observed at a certain concentration (27, 28). These changes are due to the formation of large aggregates, micelles, and the surfactant concentration at which this occurs is called the critical micelle concentration (CMC). The micelles formed in water are supposed to consist of spheres, in which the surfactant molecules are more or less radially arranged with the polar groups interacting with water and the hydrophobic groups directed towards the interior (Fig. 1a). The CMC and the aggregation number of the

micelles depend on the nature of both the hydrophobic and the hydrophilic part of the molecule.

At higher concentrations of surfactants McBain postulated the presence of a lamellar micelle (27) (Fig. 1b), while other authors found the existence of a rodshaped micelle more likely (27, 29) (Fig. 1c). A quite different model was suggested by Segerman (30). An objection, which was raised against this model when presented, was that it led to a larger contact between hydrocarbon and water than the Hartley model. The fluorine shifts of ω -trifluoro surfactants observed by Muller et al. have also been taken as evidence of the micelle interior being rather hydrophilic (11,12,13).

Since the micelle interior is oleophilic, oil-soluble substances can be dissolved in the micelle core (Fig. 2a). This phenomenon is called solubilization. Other possible ways of incorporating water-insoluble molecules in the micelles (solubilization) exist; thus the solute can be adsorbed on the micelle surface (Fig. 2b), distributed among the polar groups (Fig. 2c) or aligned parallel with the surfactant molecules (Fig. 2d). The last type of solubilizates are themselves surface active and also called cosurfactants. The isotropic phase with normal micelles is generally denoted L_1 .

Micelles of the reversed type are also formed, i.e. aggregates in which the center consists of a water core which is surrounded by the polar groups of the surfactant molecules, while their hydrocarbon chains are directed radially outwards (Fig. 3a). The formation of reversed micelles is generally favored if the surfactant has a strongly branched hydrocarbon chain. The isotropic phase with reversed micelles is generally denoted L_2 . L_2 solutions are also often observed in ternary systems composed of water, a surfactant and a cosurfactant, if the cosurfactant forms hydrogen bonds (Fig. 3b). The cosurfactant functions at the same time as the solvent.

3. NMR-parameters

3.1 The chemical shift

The resonance condition for a nucleus i is (31)

$$\nu_i = \frac{2\mu_i}{h} \cdot H_0 (1-\sigma_i) \quad (1)$$

where ν_i is the resonance frequency, μ_i the magnetic moment of nuclei of type i , h Plank's constant, H_0 the applied external field and σ_i is the shielding constant. The same kind of nuclei (same μ_i) can accordingly give resonance at different frequencies, if their electronic environment and thereby their shielding constant is different. The electronic environment is determined both by the intra- and intermolecular milieu of the nuclei.

The chemical shift, $\Delta\nu$, is the difference in resonance position, ν , for the nuclei under consideration relative to a chosen reference signal, ν_{ref} .

$$\Delta\nu = \nu_{\text{ref}} - \nu \quad (\text{Hz}) \quad (2)$$

This definition has been used in articles I-IV. - In general the definition

$$\delta = \frac{H - H_{\text{ref}}}{H_{\text{ref}}} \cdot 10^6 = \frac{\nu_{\text{ref}} - \nu}{\nu_{\text{ref}}} \cdot 10^6 = (\sigma - \sigma_{\text{ref}}) \cdot 10^6 \quad (3)$$

is preferred for the chemical shift, since the reported shifts thereby become independent of the frequency of the particular NMR instrument used. δ is generally given in parts per million and covers a range of about 20 ppm for protons and 300 ppm for fluorine-19. A negative δ thus implies that the electronic shielding is smaller in the investigated substance than in the reference substance.

3.2 Solvent shift

The contribution to the nuclear shielding from intermolecular interactions is called the solvent shift. A theory for the solvent effects in NMR spectra has been given by Buckingham, Schaeffer and Schneider (32). According to this treatment the shielding constant σ can be expressed as a sum $\sigma_{\text{gas}} + \sigma_{\text{solvent}}$, where σ_{gas} is the shielding constant for the isolated molecule in gas phase.

If the contributions from hydrogen bonding are excluded σ_{solvent} can be written as the sum (32)

$$\sigma_{\text{solvent}} = \sigma_b + \sigma_a + \sigma_w + \sigma_E \quad (4)$$

where σ_b is the effect of the bulk susceptibility of the medium, σ_a arises from anisotropy in the molecular susceptibility of the solvent molecules; σ_w is due to van der Waals forces between the solute and the solvent molecules and σ_E originates from the polarity of neighbouring molecules.

The bulk susceptibility effect, σ_b , must be taken into consideration when shifts between different samples are compared or when the shifts are referred to an external standard.

For a cylindrical sample the shift corrected for differences in bulk susceptibility, δ_{corr} , is obtained from the observed shift, δ_{obs} according to the equation

$$\delta_{\text{corr}} = \delta_{\text{obs}} + \frac{2\pi}{3} (X_v^{\text{ref}} - X_v^{\text{s}}) \quad (5)$$

where X_v^{ref} and X_v^{s} are the volume susceptibilities of the reference sample and the sample respectively.

In articles II-IV the compositions of the samples have been varied over so large concentration ranges that the difference in X_v^{s} must be accounted for before the shifts of the samples can be compared. Since the volume susceptibilities

in surfactant systems are not experimentally determined, they have to be calculated. This inevitably leads to a certain inaccuracy in the corrected shift values which might lead to obscuring of small shift effects (see e.g. ref. 33).

Anisotropy in the susceptibility of the solvent, σ_a , is generally encountered when the solvent molecules have easily mobile electrons as the π -electrons in aromatics. The aromatic molecules have their high diamagnetism perpendicular to the plane of the ring, while rod shaped molecules like acetylene or carbon disulfide have their high diamagnetism along the molecular axis.

The induced diamagnetic field of aromatic molecules is generally explained by the so-called ring current model (Fig. 4a) (34). If the aromatic ring is positioned perpendicular to the applied field, H_0 , the π -electrons will be induced to circulate in such a direction that the secondary field will be opposed to the applied field in the planes above and below the ring. However, at the positions of the aromatic ring protons this secondary field will augment the applied field. Aromatic protons therefore show resonance at comparatively low fields (7.3 ppm downfield of TMS).

Since the strength of the induced secondary field decreases with the inverse third power of the distance, it is only when the solute and the solvent molecules are in close contact that σ_a contributes significantly to σ_{solvent} of the solute. For a disc-shaped molecule like benzene a much closer contact in average is obtained between the solute and the disc in the configuration I than in the configuration II depicted in Figure 4b. This means that the diamagnetic field contribution will dominate over the paramagnetic one leading to an average decrease in the effective field felt by the solute nuclei and thus resulting in a shift to higher field of the resonance signal positions of these nuclei. The up-field shift can be of the order 0.6 to 0.7 ppm for aliphatic protons in an aromatic solvent. In paper I it is

demonstrated that the effects of the diamagnetic anisotropy of aromatic molecules give a valuable insight in the solubilization mechanism. The aromatic shifts have also been used for determination of CMC of surfactants containing an aromatic group (4, 34).

A polar group causes a polarization of its surrounding and the polar contribution, σ_E , to the solvent shielding constant, σ_s , can be approximated by (32)

$$\sigma_E = -k \frac{\epsilon - 1}{\epsilon + 1} \quad (6)$$

where k is a parameter characteristic for the solute molecule and ϵ the dielectric constant of the solvent. For protons of polar molecules in solvents with high dielectric constant the σ_E -contribution may amount to -1 ppm. The transfer of a solute molecule from a water to a hydrocarbon environment will thus result in an up-field shift for the nuclei of the solute. At micelle formation the alkyl chain protons should experience such a transfer if the micelle model with a hydrocarbon core is correct. However, the shifts observed in proton resonance at micellization are surprisingly small (IV, 9, 33). With fluorine-19 resonance CMC values have been successfully determined from shift data (11-15).

Shielding effects in hydrogen bonding are of high importance in the systems under consideration since water is present and the surface active molecules often contain groups such as -OH, -NH and -COOH, i.e. groups which are capable of forming hydrogen bonds between themselves and each other. Protons involved in hydrogen bonding exhibit a very marked deshielding.

In general both associated and nonassociated species exist in the sample at the same time. Since the hydrogen bonded protons under consideration are exchangeable, the life time of each bonding state of the proton must be larger than the reciprocal of the chemical shift between the states if separate resonance signals of the species should be observed. This is generally not the case and only an average position is observed.

As the degree of association will be both concentration and temperature dependent (e.g. the resonance signal of water is shifted about 0.008 ppm/°C) a good temperature control is of importance.

The average shift of exchanging protons is determined by

$$\delta = \sum_{i=1}^m p_i \delta_i \quad (7)$$

where δ is the observed shift; δ_i is the shift characterizing sites of type i , p_i is the population number at the site i and m the number of different types of sites.

In the surfactant solutions the molecules dispersed in the intermicellar solution and the micelle forming molecules are exposed to slightly different chemical surroundings and thus their chemical shifts can be expected to differ. However in all NMR investigations of isotropic surfactant solutions hitherto reported only one resonance signal is observed for each type of equivalent nuclei (I-IV, 1-16). This fact indicates that the exchange rate of molecules between micelles and intermicellar solution is rapid enough to cause a complete coalescence of the signals from the different environments. The exchange-averaged shift, δ , for any particular kind of nuclei in the molecules is accordingly determined by

$$\delta = \sum_{j=1}^l p_j \delta_j \quad (8)$$

where p_j in this case is the fraction of molecules bound in aggregates of type j and δ_j is the shift in this type of aggregates and l the total number of aggregation states in the system. Equation 8 is valid both for the solubilize molecules and the more directly micelle-forming molecules as the surfactant ions.

To be able to calculate the chemical shift δ_j characteristic for the micelle milieu one has generally used the simple phase separation model for the formation of micelles. This model contains the idealized assumptions that the micelle aggregation number, m is large compared to unity and is identical for all micelles and is independent of the total surfactant concentration, $[S_o]$, in the system, that the effect of the associated counterions can be neglected, and that the concentration of free surfactant (S) remains constant and equal to that at the CMC above CMC. Even if conclusions based on this model cannot be strictly correct, the model has shown to be a good first approximation. If the CMC is defined as

$$CMC = [S] = m [S_m] \quad (9)$$

where $[S]$ is the concentration of surfactant ions in monomeric forms and $[S_m]$ the micelle concentration the following relations for the observed shift can be derived.

$$[S_o] < CMC \quad \delta = \delta(S) \quad (10)$$

$$[S_o] > CMC \quad \delta = \delta(S_m) + \frac{CMC}{[S_o]} \cdot (\delta(S) - \delta(S_m)) \quad (11)$$

where $\delta(S)$ is the chemical shift of monomeric surfactant molecules and $\delta(S_m)$ that of micelle bound surfactant ions.

A plot of δ against $[S_o]^{-1}$ should accordingly consist of two straight line segments intersecting each other at $[S_o]^{-1} = (CMC)^{-1}$. Except in the neighborhood of CMC good straight line adoption is observed (9, 11, 16).

3.3 Line_Width

In an ideal experiment a sharp spike would be obtained at the resonance position of a given group of equivalent nuclei. That this is not the case depends on line broadening due to inhomogeneity of the applied field, spin-lattice relaxation, spin-spin relaxation, superimposition of unresolved lines and/or exchange broadening (34).

The width of an experimentally observed NMR signal of Lorentzian shape is defined as the width at half height and denoted, $\Delta\nu_{1/2}$. For this case an effective transverse relaxation time, T_2^{eff} , can be defined by the following equation:

$$\Delta\nu_{1/2} = (\pi T_2^{\text{eff}})^{-1} \quad (11)$$

The relaxation rate, $(T_2^{\text{eff}})^{-1}$, can be regarded to consist of two parts viz. $(T_2^{\text{app}})^{-1}$ and $(T_2^{\text{syst}})^{-1}$, where $(T_2^{\text{app}})^{-1}$ is connected with the broadening of the NMR line caused by the apparatus (e.g. field inhomogeneity and saturation), and $(T_2^{\text{syst}})^{-1}$ the one caused by the chemical system (e.g. dipole-dipole interactions and chemical exchange). In liquids of ordinary viscosity molecular motion is so rapid that motional averaging is complete and the dipolar broadening will be negligible. This will be the case when the condition

$$2\pi\nu_0 \tau_c \ll 1 \quad (12)$$

is fulfilled where ν_0 is the resonance frequency and τ_c the correlation time. In those cases the spin-lattice (T_1) and the system transverse (T_2^{syst}) relaxation time will be equal if the exchange broadening is negligible.

$$T_1 = T_2^{\text{syst}} \quad (13)$$

If only pairs of protons are considered (36)

$$\frac{1}{T_1} = 6 \cdot \left(\frac{\pi}{h}\right)^2 \cdot \mu^4 \cdot \frac{\tau_c}{r^6} \quad (14)$$

where μ is the magnetic moment and r is the distance between the nuclei.

If the molecule is regarded as a rigid sphere with radius a embedded in a liquid of viscosity, η , the correlation time τ_c is given by

$$\tau_c = \frac{4\pi \cdot a^3}{3k} \cdot \frac{\eta}{T} \quad (15)$$

In general the resonance lines of the various types of protons in the surfactant molecules are not much broadened due to the formation of micelles (2, 6). This indicates that the molecular motion is rather rapid in the micelle. If large rod-shaped micelles are formed a significant broadening is, however, observed (1, 6). The changes in the relaxation times of the protons (or fluorine nuclei) in the hydrocarbon chains which do occur at micelle formation have to be determined by spin-echo or similar methods. Studies by Clifford et al. (22-24) thus showed that the relaxation rate of the CH_2 -protons in the interior of sodium dodecyl sulfate micelles is $2.0\text{-}3.3 \text{ sec}^{-1}$, which should be compared with the relaxation rate in dodecane 0.5 sec^{-1} and in glycerol tridodecanoate 6.0 sec^{-1} .

The superimposition of unresolved lines can also give rise to changes in the line width of the apparent one-line signal. For example, the CH_2 -peak from the hydrocarbon chain of an amphiphilic molecule is a comparatively broad signal due to the fact that the CH_2 -groups along the chain have only slightly different chemical surroundings, while a ^{13}C -spectrum of the same molecule will consist of several resolved peaks (16, 17). The presence of two different kinds of amphiphilic molecules with slightly different average chemical surrounding can also cause changes in the width of the " CH_2 -peak" (III). Various degrees of resolution of hyperfine structure can also show itself as alterations in the half-width of the signal (II).

3.4 Nuclear Quadrupole Relaxation

A comprehensive treatment of the applications of quadrupole relaxation to the study of counterion binding in surfactant systems is given by Lindman (37).

In case of extreme narrowing, the line width, ΔB is given by

$$\Delta B = K \left\langle (\delta^2 V / \delta z^2)^2 \right\rangle \tau_c \quad (16)$$

where K is constant characteristic for the nucleus $\langle (\delta^2 V / \delta z^2)^2 \rangle$ is the mean square electric field gradient at the nucleus and τ_c is the correlation time which characterize the rate of reorientation of the field gradient tensor.

If the nuclei exchange rapidly between several sites of different types i and the rate of exchange is sufficiently rapid to give rise to one single coalesced NMR signal the observed line width, ΔB_{obs} , is given by

$$\Delta B_{\text{obs}} = \sum_i p_i \Delta B_i \quad (17)$$

where p_i is the population fraction of nuclei at sites of type i characterized by the line width ΔB_i . In paper V the ^{81}Br resonances in systems of serum albumin and surfactants have been analyzed according to equation 17.

4. Solubilization

The increased solubility of oleophilic substances, which is obtained in micellar solutions, has many practical applications. In the pharmaceutical utilization changes in the activity of the solubilized drugs have often been noted (28). These changes might partly be due to specific substrate-micelle interactions. The catalytic effect on organic reactions by micelles (8, 38-40) have further increased the interest in the solubilization sites of different substrates.

In paper I the solubilization sites of aromatic compounds in cetyltrimethylammonium bromide micelles is discussed from PMR and viscosity data. Due to the diamagnetic anisotropy of the aromatic ring the proton shifts observed are significant. By extrapolating the shifts of the solubilize protons to zero concentration we could conclude that benzene, N,N -dimethylaniline and nitrobenzene exist in an aqueous environment in the micelle at low and intermediate concentrations. From the shifts of the surfactant resonances the

changes in line width and viscosity we concluded that the most probable solubilization site was close to the α -CH₂-groups of the CTAB-molecule.

An earlier study by Eriksson (2) showed that the same solubilization mechanism exists in cetylpyridinium chloride micelles, and one by Nakagawa and Inoue (5) that the extrapolated signal position of benzene solubilized in sodium dodecylsulfate micelles nearly corresponded to that of benzene in water.

Later PMR investigations by Gordon et al. (41), Fendler et al. (40, 42) and Jacobs et al. (43) have confirmed that the first added aromatic molecules are solubilized in an aqueous environment in micelles formed both by anionic [sodium dodecanoate, sodium dodecylsulfate (NaLS)], nonionic (polyoxyethylene(23)laurylether) and zwitterionic [3-(Dimethyldodecylammonio)propane-1-sulfonate (DDAPS)] surfactants. Although these authors favor the interpretations of paper I, they point out the fact that the extrapolated benzene shifts per se cannot be considered as evidence that the solubilization site for benzene is at the surface of the micelle, since the results of Müller et al. (11-13) might indicate that water exists in the micelle interior. By calculating the order of change in chemical shift as a function of benzene concentration for the surfactants Fendler et al. (42) found that the dynamic solubilization site of benzene is near the surface for CTAB and DDAPS micelles but closer to the interior in NaLS micelles. Reactivity differences of benzene with e_{aq}^- in these two micellar systems agree with this interpretation (42).

Müller and Birkhahn (11) introduced the parameter Z for characterizing the medium bathing a surfactant or solubilize molecule. Z is defined as

$$Z = \frac{\delta_{micelle} - \delta_{aq}}{\delta_c - \delta_{aq}} \quad (18)$$

where $\delta_{micelle}$ is the chemical shift of the protons or the

fluorine nuclei within the micelle, δ_{aq} in an aqueous solution and δ_c in a hydrocarbon or fluorocarbon medium. A Z-value equal to zero thus implies a pure water environment; and one equal to 1 a pure saturated hydrocarbon or fluorocarbon. For solubilized benzotrifluoride they found a Z-value of 0.5 in sodium caprate micelles, of 0.5-0.6 in sodium laurate and 0.6-0.7 in the micelles formed by the soaps with an ω -trifluoromethyl group.

Gordon et al. have calculated the Z-value for benzene in polyoxyethylene(23)laurylether, CTAB and sodium decanoate micelles and find them to be 0.06-0.16, 0.18 and 0.29-0.33 respectively (41). The results of Fendler et al. and Gordon et al. thus indicate that the interior of an anionic micelle offers a rather hydrophilic environment for solubilized benzene. However, in a preliminary PMR-investigation of solubilized benzene in a micellar solution (0.173 M) of sodium n-dodecylbenzenesulfonate, the extrapolated shift of benzene corresponded to that in cyclohexane (44).

The chemical shifts of cyclohexane in the CTAB-micelles is about the same as in pure cyclohexane (I) and at high concentrations the shifts of the aromatic solubilizates approach that in the pure hydrocarbon (I).

Under these conditions the micellar environment of the solubilizate molecules is predominantly hydrophobic. Results from differential UV spectroscopy support this interpretation (42, 48). The hydrophobic surrounding might, however, depend on a perturbation of the micelle structure, in terms of size and shape, by the presence of the solubilizates (I, 40) or on a formation of a core of the solubilizates molecules in the micellar interior (I).

In the period passed since the examinations in paper I were made, Fourier transform NMR instruments have become available enabling ^{13}C NMR studies on the natural abundant carbon-13. As illustrated by Drakenberg and Lindman (16) and

William et al. (17) the chemical shifts of the different carbons in the hydrocarbon chain of the surfactant molecule can be observed separately. It seems, therefore, very credible that a ^{13}C NMR study of the solubilization systems would allow a more final conclusion of the solubilization sites and their degree of hydrophobicity than the fluorine and proton NMR data presently available.

5. Reversed micelles

Paper II is the third article in a serie aiming to elucidate the properties and structure of the L_2 -region in the sodium caprylate-decanol-water system (46, 47, II,19). The investigations of Ekwall (46, 47) showed that the right boundary of the L_2 -region (see Figure 1, paper II) for different alkali soaps correlated well to the hydration number of the used alkali ions at the given temperature. At 30°C the right boundary for the L_2 -phase in the sodium caprylate-decanol-water system corresponds to 5.4 moles of water per mole of sodium caprylate. The maximum water content at the left border is about 27 moles of water per mole of sodium caprylate. This limit was assumed to depend on the amount of water, which could be bound to the hydrophilic groups of the micelle forming molecules which were shown to be both caprylate and decanol molecules. Density and viscosity measurements and X-ray diffraction observations showed that micelles were formed at about 90% decanol and that uniform spherical micelles were formed at a lower decanol content.

The NMR investigation (II) was performed to see if further support for these interpretations could be obtained. Although the observed changes in the chemical shifts of the various protons, except the exchanging OH-protons, were rather small, the analysis of the results supported the earlier conclusions.

A few determinations of the resonance line width of the ^{23}Na -counterions were also made. Later, this investigation was extended by Lindman (19). Regarding the results of Lindman

(19, 20) and also those of Robb (21) a modification of the interpretation in paper II seems motivated to-day.

Lindman (20) found that the line width of a sodium ion covalently bound to caprylate ion is of an order a hundred times larger than the greatest line-width found in sodium caprylate-decanol-water system. Hence, even in the solutions with the lowest water to sodium caprylate ratios, it is most plausible that all of the sodium ions are approximately totally hydrated. The sodium ions are accordingly linked via water molecules to the carboxylate groups of the soap.

For normal micelles Robb (21) found that changes in relaxation rate was mainly determined by a change in electrical field gradient. He suggested two possible mechanisms, which might alter the electric field gradient viz. i) an increase in the rate of exchange of water molecules between the bulk and the hydration layer of the ion and ii) the bending or distortion of the symmetrical arrangement of the water dipoles around the ion. Of these two possibilities he favored the latter one. It also seems most credible that the latter mechanism is responsible for the increased line widths observed in the systems in paper II and reference 19.

In the systems with a molar ratio of water to sodium caprylate of 5.9 the majority of the water molecules forms the hydration layer of the sodium ions. The relatively high resonance line positions calculated for the CH_2 -dec, the $\alpha\text{-CH}_2$ -dec and the $\alpha\text{-CH}_2$ -NaCy protons (see Table 1, paper II) also confirmed that a very little penetration of water molecules to these groups took place.

In the mesomorphic F-sample two overlapping signals were observed at 30.5°C for exchanging OH-protons. An alternative explanation to this phenomenon is that equilibrium conditions had not been obtained and hence the sample contained both a F-phase giving rise to the broad signal and a L_2 -phase giving the narrow signal. Separate water signals in the same sample have been observed for systems containing both solubilized and emulsified water (48, 49).

6. Microemulsions

The concept of microemulsions was introduced by Hoar and Schulman in 1943 (50). They found that the turbid emulsion (Fig. 5, B) formed when an alkali soap was added to benzene and water (Fig. 5, A), became transparent (Fig. 5, C) when a second amphiphile, such as an alcohol of medium chain length, was added above a certain concentration. However, these microemulsions are easily differentiated from ordinary emulsions not only due to their transparency but due to the fact that they represent a thermodynamically stable one-phase system in opposition to the unstable two-phase systems of ordinary emulsions. A microemulsion would accordingly be more correctly denoted by an oil/water or water/oil micellar solution. The name of microemulsion is, however, advantageous to keep as a concept for the solubilized micellar systems with high contents of both oil and water. In the review on microemulsions recently written by Shinoda and Friberg (51), a more general discussion of these different opinions of microemulsions is given.

In paper III the colloidal aspect of microemulsions is proved. We thus show that, in the L_2 -solutions formed in the system potassium oleate-hexanol-water, benzene could be dissolved in sufficient amount for the solutions to be named microemulsions. As a matter of fact, microemulsions with identical composition to Schulman's microemulsions could be obtained in this system. Further more these microemulsions could be reached by starting with the pure benzene and adding to it first hexanol and then water and potassium oleate. The additions to the solution took place without observation of a phase transition. Regarding this fact the advantage of considering the microemulsions as anything but colloidal solutions appears limited.

If benzene is added to the system potassium oleate-hexanol-water the solubility area of the L_2 -solution increases to reach a maximum at a benzene content of about 40% (w/w).

Higher amount of benzene than 60% leads to a rapid decrease in the quantity of water, which can be dissolved by the potassium oleate and hexanol. By comparing shape changes in the methyl and methylene signals and by analyzing the observed chemical shifts of the exchanging OH-protons and by IR-investigations, a possible explanation of the variations in the region of existence of the microemulsions at different levels of benzene could be given. The distribution of hexanol between micelles and intermicellar solution seems to be the decisive factor.

Some indications of an exchange broadening of the OH-proton signal are considered in the paper. However, changes in the viscosity, either the macroscopic or the microscopic one, would give a similar effect. Small changes in the macroscopic viscosity do occur. Until careful measurements of the viscosity have been performed it is impossible to rule out any one of the mechanisms.

7. Special Isotropic Phases

In some systems of water, a surfactant and a third component, which might be an amphiphilic substance or a hydrocarbon, one and the same isotropic solution can vary in its water content from 0 to 100% i.e. a L_1 -phase with normal micelles might change continuously to a L_2 -phase with reversed micelles (III, IV, 26, 38). Of special interest is to try to find out the micellar structure in the transition region.

The ternary system n-octylamine-p-xylene-water is an example of a system containing these special isotropic phases (IV). The association conditions in this system is also of interest since it consists a part of the quarternary system water - n-octylamine-caprylic acid-p-xylene which has proved to be suitable as a model system to study emulsion stability (52). An IR and X-ray investigation has been made of the subsystem water-n-octylamine-caprylic acid (53) and an IR and NMR investigation of the subsystem n-octylamine-caprylic acid-p-xylene (54).

In one of the series examined in paper IV the water content was varied from 0 to 100%. The molar ratio of the p-xylene to n-octylamine was kept approximately constant up to a water content of 80 mole %. At higher water contents this was not possible since the water wedge here is very narrow.

Light scattering data, chemical shifts and line widths of the different protons indicated that one change of aggregate structure took place when the water content exceeded 65-75 mole % (20-30% (w/w)) and another one when the water content exceeded 94 mole % (70% (w/w)). The light scattering ratio showed that the aggregates first formed on the addition of water were rather small and of approximately constant size, that those existing in the region 30-70% (w/w) of water increased in size and that a very rapid increase in the size of scattering units was obtained at water contents larger than 70% (w/w). The PMR results suggested that the first formed aggregates contain water which was more hydrogen bonded than ordinary water, that those in the region 30-70% (w/w) might be of a lamellar type and that the increase in aggregate size at water contents larger than 70% (w/w) mainly originated from the simultaneously occurring decrease in the xylene content.

In the investigations of the isotropic phase formed in the CTAB - butanol - buffer system where the buffer was a 0.01 M sodium phosphate solution with pH 11.5 the water content was varied from about 10 to 100 weight percent in a series studied by ^{81}Br NMR and light scattering (38). In this system the intensity of scattered light was low up to a water content of 40% (w/w) and the line widths of the ^{81}Br resonance (ΔB) too high to be conveniently determined. In the region of 40-60% (w/w) water ΔB rapidly decreased and the scattered intensity increased, in the region of 60-70% (w/w) water both factors were rather constant. Sharp decreases in the 70-80% (w/w) water range were followed by less pronounced reductions at higher water contents.

Since pure butanol could dissolve up to 20% (w/w) water and up to 15% (w/w) CTAB, and normal micelles exist in water - CTAB solutions up to a CTAB content of about 27% (w/w) the results in this investigation were interpreted as follows:

In the region about 40% (w/w) water association into micellar aggregates of reversed structure took place. The transition to normal micelles occurred in the region of 60 to 70% (w/w) water i.e. in the region, where ΔB and scattered light were constant. Investigations with low-angle X-ray diffraction showed no signs of multilayer structure in any water range. Micelles containing separated layers did not exist in the transition range in this system. However, no lamellar crystalline phase is formed in the CTAB - butanol - water system in opposition to the CTAB - hexanol - water system. Micelles of monoglycerides in a triglyceride solution have on the other hand been shown to consist of several lamellar layers (38).

A comparison between the results in reference 38 and those in paper IV shows that the micelles formed in the two systems are quite different. This difference probably originates from the fact that CTAB is water soluble while octylamine dissolves in water only to a very slight extent.

The very small aggregates of water and octylamine formed up to a water content of 30% (w/w) might either be small reversed micelles or complexes between water and octylamine.

Since a water content of 30% (w/w) corresponds to a molar ratio of water to octylamine of 2 to 1 a complex binding of the water is within the binding ability of the amino group.

8. Protein - surfactant interaction

Nuclear quadrupole relaxation has been shown to provide excellent possibilities for studying the function of proteins and protein interaction with various ions. The application

is limited to those proteins interacting with small ions such as the halide ions which can act as probes due to their non-zero quadrupole moment (37). When such a protein is dissolved in a water solution containing halide ions various types of binding sites will exist for the ions. They can, for example, be "free" in the solution or coupled to cationic groups in the protein. In the case of rapid exchange the observed line width will be determined by equation 17 and, accordingly, variations in binding condition will cause changes in the observed line width.

It is well established that serum albumin belongs to these proteins which bind halide ions by ionic interaction with positive sites on the albumin molecule (55). Serum albumin has also been extensively used for studying interactions of surfactant ions with proteins. The binding of anionic surfactants is supposed to occur via ion-pair formation with cationic sites on the protein, but a hydrophobic interaction is also suggested. If a hydrophobic interaction occurs conformational changes in the protein molecule can be expected. In both cases changes of the binding conditions for the halide ion ought to result, in the first case by a direct displacement of the halide ions by the surfactant anions, and in the second case by changes in the environment of the binding sites due to the conformational changes. Since the nuclear quadrupole relaxation of halide ions has proved to be an excellent probe in other types of protein interactions (37) we determined to investigate its applicability for studies of protein - surfactant interactions. The results of this study is given in paper V and they showed that the suggested method indeed can be used for evaluating protein - surfactant binding.

In this investigation 0.5% (w/w) human serum albumin was dissolved in 0.167 M potassium bromide buffered to pH 5.6 and the line width of the ^{81}Br resonance signal was studied as a function of the amount surfactant added. The surface active agents used were sodium alkylsulfates (C_4 , C_8 and C_{12}),

sodium octylsulfonate, sodium caprylate, nonyl-trimethylammonium bromide (NTAB) and the hydrotrop sodium o-xylene-4-sulfonate.

All the anionic substances caused a decrease in the line width. From the observed differences we could confirm that the affinity of the anionic surfactant ligand increased with increasing chain length. Variations in the anionic group had less an effect on the displacement ability of the surfactant. The cationic surfactant (NTAB) did not at all effect the line width of the bromide signal.

By means of equation 17 a calculation of number of sites per HSA unit and the line width of the ^{81}Br signal characterizing these types of sites was performed. The site numbers agreed well with those obtained by other methods.

In a later publication by Magnuson and Magnuson (56) ^{35}Cl NMR was used for studying surfactant binding to bovine serum albumin (BSA). These results agree well with those in paper V. Thus, they found from the changes in the line width of the ^{35}Cl resonance signal, that the effectiveness in displacing chloride ions from BSA followed for sodium alkyl-sulfates the order $\text{C}_{12} > \text{C}_{10} > \text{C}_8 > \text{C}_6$ and that the cationic surfactant, cetyltrimethylammonium bromide and the nonionic surfactant Triton X-100 did not at all influence the interaction of the chloride ions with BSA.

Both the results in paper V and in reference 56 indicate that anionic surfactants compete for the same binding sites as the halide ions. The increased displacement ability with increasing length of alkyl chain of the surfactant might be taken as an indication that the surfactant hydrophobically interacts with the protein besides taking part in ion-pairing. However, even with such a hydrophilic polymer as heparin, which is a mucopolysaccharide with an average of one sulfate group per dimer unit, it has been observed that there is an increased strength in the complexes formed between heparin and cationic surfactants with increasing length of the alkyl chains (57).

A C K N O W L E D G E M E N T S

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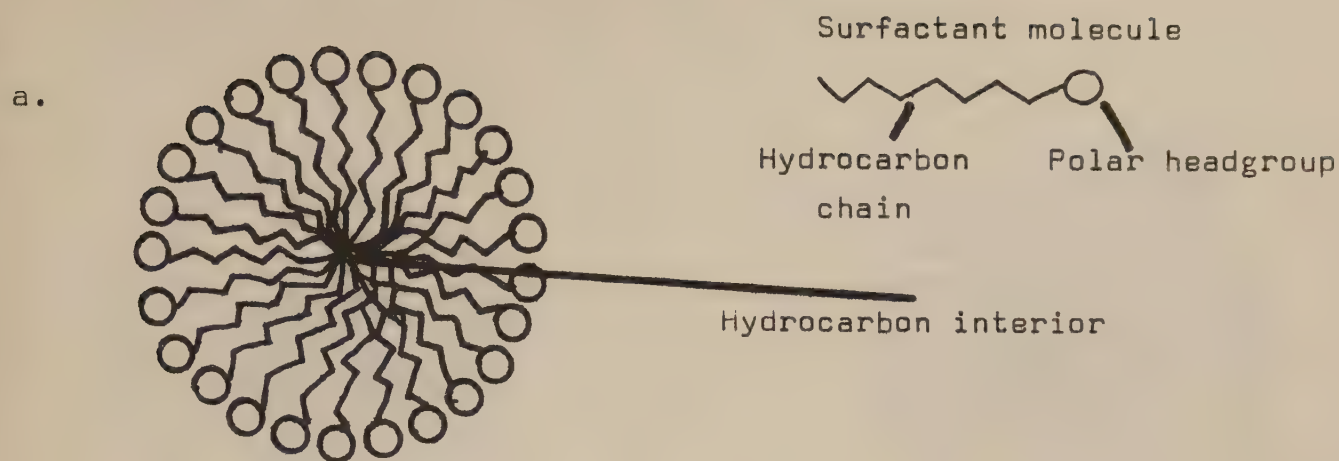
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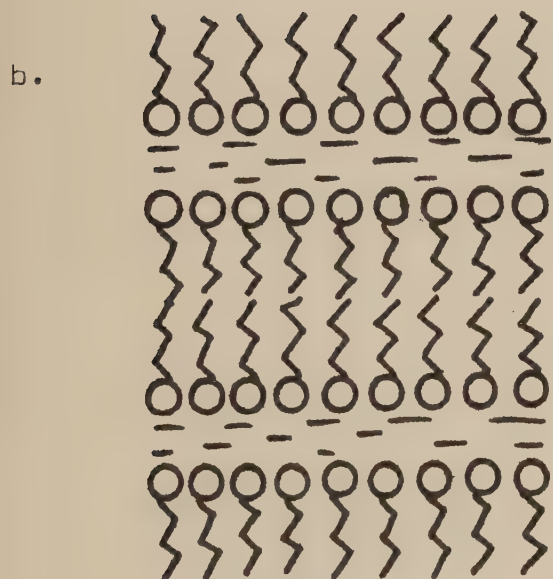
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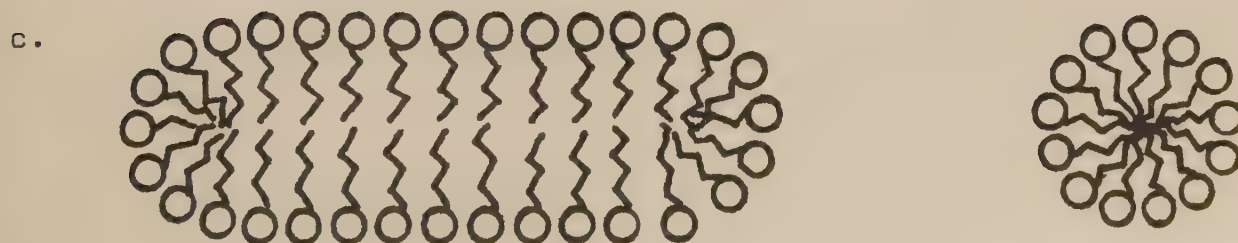
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THE HARTLEY SPHERICAL MICELLE

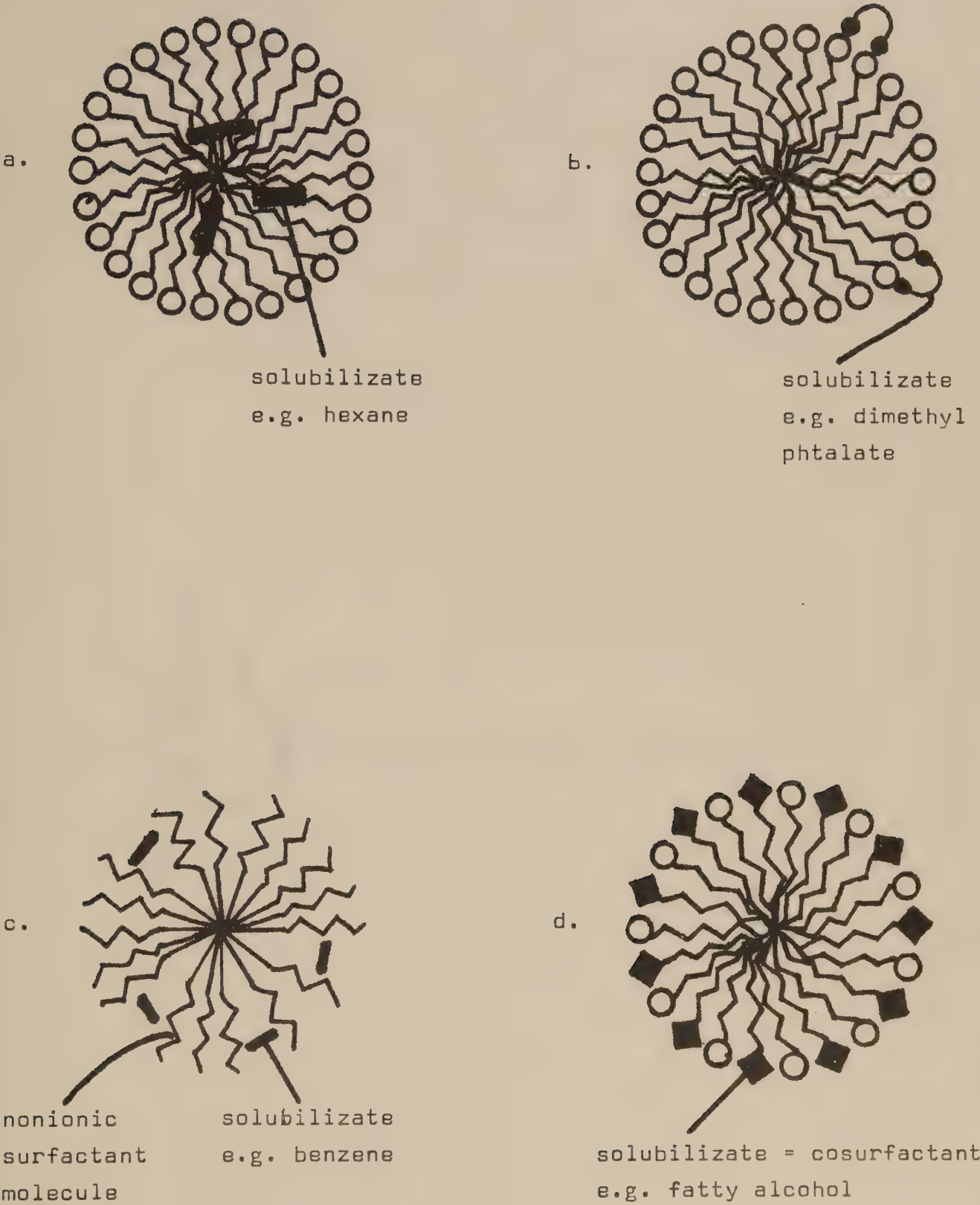


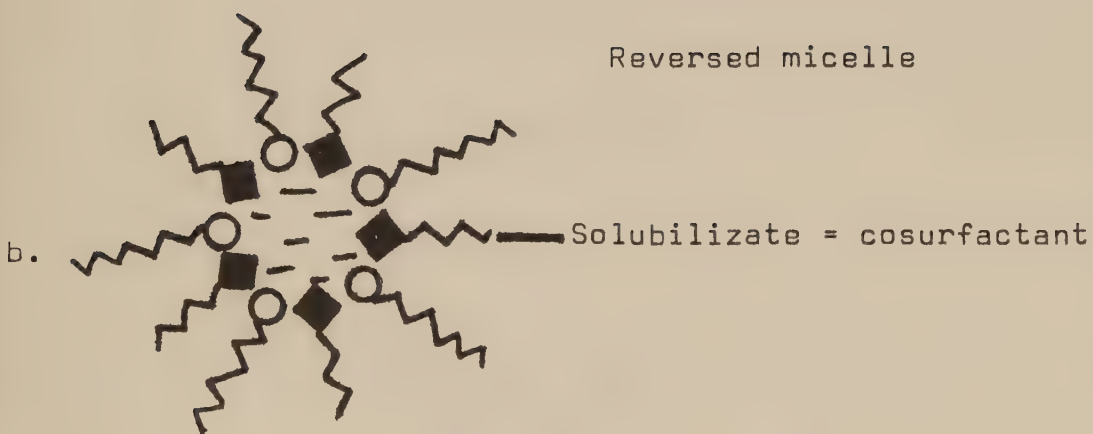
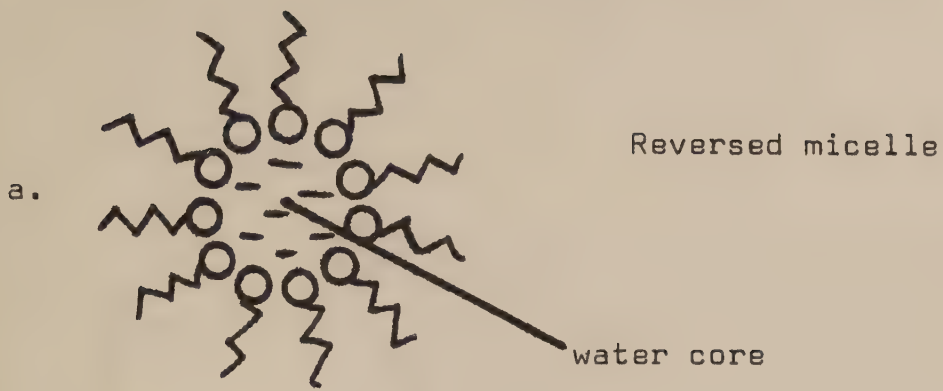
THE McBAIN LAMELLAR MICELLE

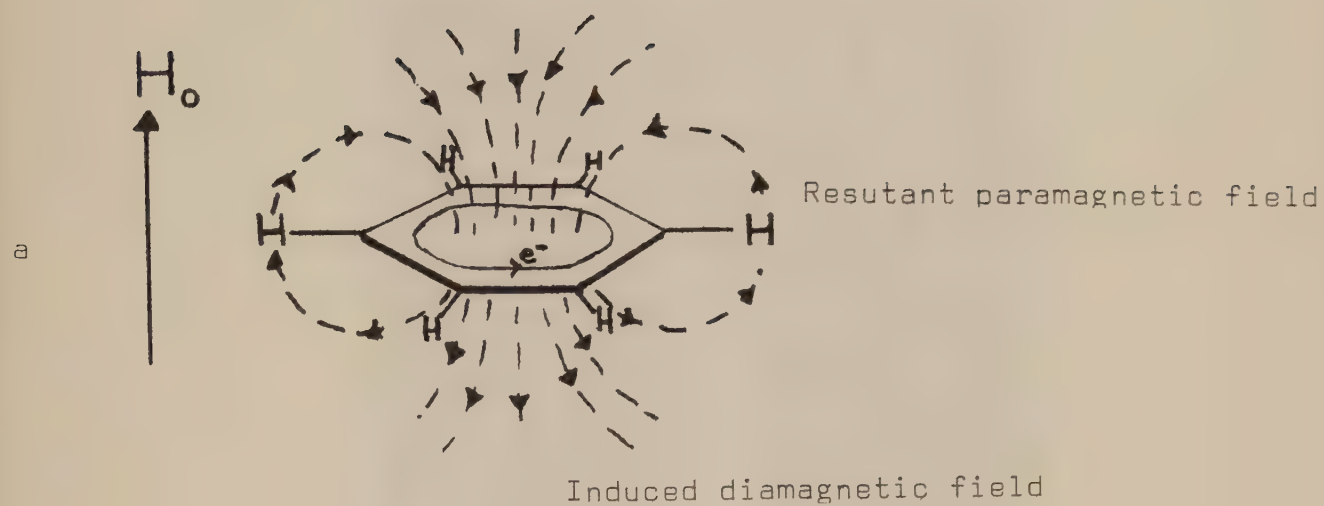


THE DEBYE RODLIKE MICELLE

DIFFERENT SOLUBILIZATION MECHANISMS





DIAMAGNETIC ANISOTROPY OF THE
AROMATIC RING

SOLUTE-DISC CONTACT

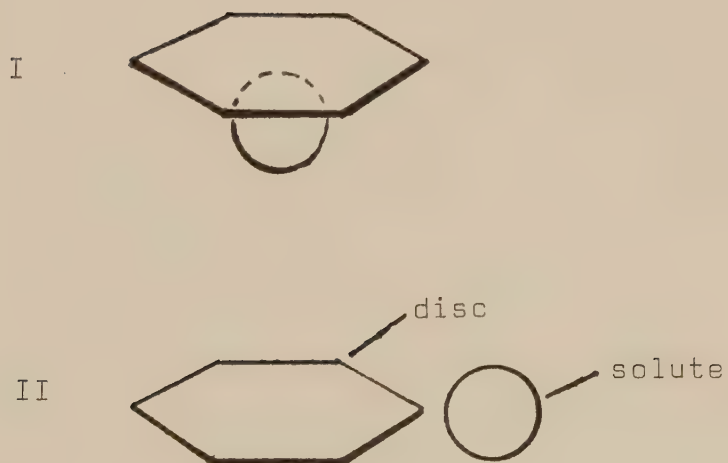
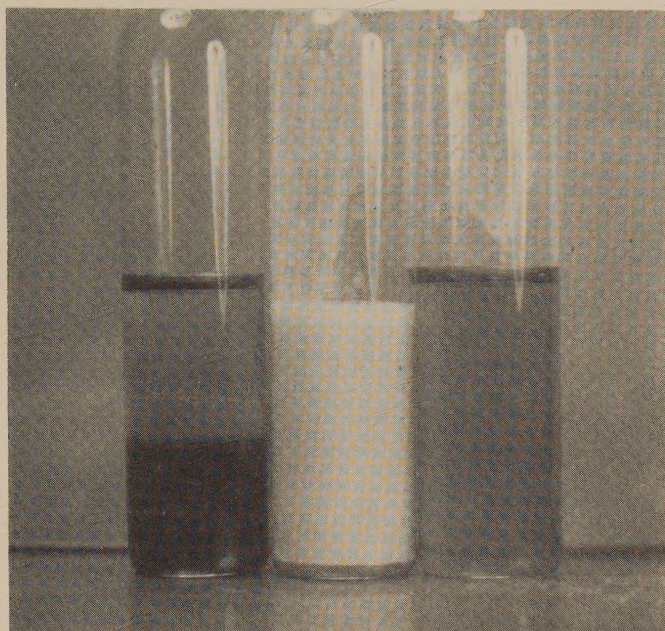


FIGURE 5



A

B

C



YTKEMISKA INSTITUTET